Modern Concepts of Cardiovascular Disease

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DYSPNEA*

The subject of dyspnea has been reviewed following each major advance in respiratory or pulmonary physiology.[1-4] The recent development of objective tests for the evaluation of pulmonary function in man[5,6] has created fresh interest in the origin, mechanisms and treatment of dyspnea. This report is an inquiry into some of the still unsolved fundamental problems: (1) What is dyspnea? (2) What is its origin as a sensory experience? (3) Is there a single neurophysiologic mechanism which will explain the sensory experience?

1. What is dyspnea?

Is it a symptom or a sign? I believe we should continue to use the word dyspnea to connote a *symptom*, a sensory experience which, like pain, can be perceived and judged only by the patient. The use of the recently introduced term "objective dyspnea" (a decrease in ventilatory reserve below the range of healthy persons when compared at the same level of activity), is inadvisable because it implies that the important factors in the causation of dyspnea have been identified and relate to a specific decrease in ventilatory reserve. This is not necessarily true.

It might be profitable to compare the symptom, *dyspnea,* with the symptom, *pain.* Pain can be characterized by an instructive variety of terms such as stabbing, throbbing, aching, burning, oppressive or bursting. However, the patient's description of *respiratory* distress is channeled by most physicians into two terms: "dyspnea" and "shortness of breath." More precise recording of the patient's own characterization of his difficulties in breathing might lead to better correlation of these with objective tests of pulmonary function or with mechanisms responsible for the dyspnea. Is the kind of respiratory discomfort experienced in acute respiratory obstruction, emphysema, congestive heart failure, pulmonary embolism, acute neuromuscular paralysis, anemia, acidosis, neurocirculatory asthenia, or pulmonary fibrosis, really identical in each? How much of the distress is pain, how much is fatigue or exhaustion, how much muscular aching, and how much is apprehension or fear?

2. What is the origin of dyspnea as a sensory experience?

If we agree that dyspnea is a symptom just as pain is a symptom, there must be a neuroanatomical basis for it. Like pain, there may be only a central basis or there may be both peripheral and central components. Therefore, we must look for the sensory receptors, sensory pathways and thalamic or cortical centers which are responsible for the perception of respiratory discomfort and for the reaction to these unpleasant stimuli. Again, just as some patients have little pain (minimal sensory stimulation) but suffer greatly (maximal central response), or have much pain and suffer little,[7] similarly some patients might have little respiratory difficulty and much dyspnea, or much respiratory difficulty and little dyspnea.

3. Neurophysiological mechanism

What and where are the sensory *receptors* which initiate afferent impulses leading to dyspnea? Are they the same mechanoreceptors or chemoreceptors involved in the normal processes of breathing—those which regulate the rate and depth of respiration? Is dyspnea caused by a barrage of impulses from these directed to the medullary respiratory center which, when in excess, spill over into the areas of consciousness? Is it caused by the activation of special receptors, not normally tonically active, which send impulses directly to the centers of consciousness and not primarily to the respiratory center? Or is it caused by a change in the pattern of impulses—too few of some, too many of others, or an asynchrony of several (cf. dysaesthesia)? Are these receptors located in the tissues surrounding the airway, in the alveoli, the pulmonary circulation, the pulmonary parenchyma, the pleura, the bones, joints or ligaments of thoracic cage, or in the muscles of respiration? Are they receptors for touch, change in temperature, in pressure or tension, in stretch, distention, volume or position, or in chemical compo-

*From the Department of Physiology and Pharmacology, Graduate School of Medicine, University of Pennsylvania, Philadelphia, Pa.

sition? Do their afferent fibers run centrally in the vagi, in the sympathetic nerves or in the somatic nerves?

No one knows the answers to these questions at the present time and little active investigation has been directed toward their solution. Rather, the attempts to determine the nature and origin of dyspnea have centered on correlating the degree of dyspnea with something that can be measured in man, i.e., dyspnea in relation to changes in vital capacity, maximal breathing capacity, breathing reserve, arterial O_2 or CO_2 tension, minute volume of ventilation, the degree of stretch or collapse of the lungs, or to O_2 consumption. Almost all investigators have attempted a unitarian explanation but none of their explanations is free from major criticism if it is intended to present the sole or important cause of all or most types of dyspnea.

Within the past 5 years, it has become possible to make reasonably accurate measurements of all of the important forces and resistances involved in the act of breathing.[8-11] These include the measurement of compliance, airway resistance, pulmonary nonelastic tissue resistance and the total work of breathing. *Compliance* is a measure of the distensibility of the elastic components of lung tissue, expressed as liters of volume change for each cm. H_2O pressure change acting on the lung. A rather formidable measurement in the past because it involved the direct determination of intrapleural pressure, compliance is now relatively easy to estimate, employing the indirect measurement of changes in intrapleural pressure by the use of an intraesophageal balloon. *Pulmonary resistance* also can be measured by modern techniques as (a) the frictional resistance offered by the pulmonary tissue to deformation, and (b) the frictional resistance to the flow of air into and out of the hundreds of thousands of fine and large tubes that make up the conducting airway.[12,13] The *total work of breathing*, which is the work done in moving the thorax, lungs and air, and the work involved in moving the lungs and air alone, can also be measured. These measurements permit for the first time a correlation of the severity of the symptom of dyspnea with objective values for the forces and resistances in the breathing act, and this in turn permits clinical physiologists to test a rather attractive theory of the causation of dyspnea which is based on the effort required in breathing. This concept states that dyspnea, like the pain of intermittent claudication or of angina pectoris, occurs when the work of the respiratory muscles is great relative to the flow of oxygenated blood through these muscles; as a result chemical products of metabolism accumulate to a level which excites sensory nerve endings in muscle, thus producing dyspnea. This concept could explain dyspnea associated with cardiopulmonary conditions in which pulmonary or thoracic compliance is reduced, or in which tissue or airway resistance or both are increased. It could also explain the dyspnea of hyperventilation, of exercise, or of anemia in which there is either increased thoracic muscular activity or decreased O_2 supply to the respiratory muscles or both.

Unfortunately, increase in muscle *work*, using the strict definition of the physicist, cannot be correlated well with dyspnea because "work" involves both force and the distance through which it acts. Thus, violent breathing efforts against a completely obstructed airway would involve little or no "work" (little or no distance) even though the O_2 consumption of the muscles would rise sharply. Until the physicist devises an acceptable term for work which includes static effort, it is probably better to relate dyspnea to the *force* acting on the lung[14] or to the extra O_2 consumption caused by respiratory effort.[15]

Several laboratories are now engaged actively in a study of the mechanical factors in breathing and their relation to dyspnea. Difficulties may be predicted in the effort to establish this new unitarian concept because of certain observations:

(a) The subjective reaction to increased respiratory effort may vary widely. One of our patients had severe pulmonary insufficiency for both O_2 and CO_2 (arterial O_2 saturation 72 per cent; arterial CO_2 tension 63 mm.Hg), marked reduction in lung volumes (vital capacity 690 ml.; total lung capacity 2550 ml.) and the lowest value for maximal breathing capacity (11 L./min.) ever encountered in our laboratory. However, she never complained of dyspnea even during mild exercise on the treadmill.

(b) Patients with severe weakness of the respiratory muscles caused by poliomyelitis or intercostal neuritis may suffer intense dyspnea at times when their respiratory muscles are doing little or no work and exerting little or no force on their lungs.

(c) Subjects receiving curare to the point of paralysis of the respiratory muscles may experience dyspnea even when pulmonary ventilation, achieved by positive pressure applied to the airway, is adequate.[16]

(d) Patients undergoing high spinal anesthesia may have the sensation of dyspnea at a time when superficial thoracic sensations are lost but voluntary movements of the thoracic cage appear to be unimpaired.

(e) Patients with neurocirculatory asthenia complain of dyspnea, although no major alteration in the mechanical factors in breathing has yet been demonstrated.

(f) Subjects who have held their breath to the breaking point can continue for a longer time if a short period of breathing is permitted, even though the gases then breathed are low in O_2 and high in CO_2.[17]

(g) Paralyzed patients receiving adequate alveolar ventilation in a body respirator may develop dyspnea which is relieved by producing an occasional deep inspiration. Such dyspnea may have resulted from insufficient inhibitory impulses

from stretch receptors, or from an excessive barrage of excitatory impulses caused by small areas of collapse (insufficient stretch).

(h) Dyspnea may be severe if a breathing tube is occluded abruptly without warning the patient, but may be inconsequential if the patient if asked to occlude the tube himself for the same period of time.

(i) Patients with acute embolism of a pulmonary artery may suffer severe dyspnea, although the ischemic type of pulmonary embolism theoretically should not be associated with significant changes in the mechanical properties of the lungs.

Summary and Conclusions

There is an amazing lack of precise information regarding the origin of one of the commonest symptoms encountered in clinical practice. Theories of the genesis of dyspnea should be supported or disproved by more direct experimentation. This should include an extension of current studies of the mechanical factors in breathing with further measurements of respiratory work, pulmonary and thoracic compliance, nonelastic tissue resistance and airway resistance in patients with dyspnea. However, investigators might also do well to direct their attention to determining the neurological basis of dyspnea. This might be achieved by the study of patients who require, for some proper medical reason, interruption of nervous pathways by surgical means or by blocking procedures; this might include patients subjected to thoracic sympathectomy or operations on the central nervous system for the relief of pain. It might be aided by more complete study of those unfortunate individuals who suffer from various motor and sensory paralyses affecting the thorax. It might even involve the study of action potentials in respiratory muscles, the use of differential spinal anesthesia, temporary vagal nerve block or anesthetization of the airways by aerosols (with full realization of the dangers involved) in an attempt to learn more about the nervous pathways for dyspnea.

One might predict that study will reveal eventually that there are multiple factors in the causation of dyspnea and that in certain cases dyspnea will exist with no measurable changes in the physical properties of the lungs by present tests. One might also predict that in the great majority of patients with dyspnea, the physiologist will be able to identify and quantify alterations in the mechanical factors in breathing, and that more widespread use of the newer tests of pulmonary function will bring us nearer to an understanding of dyspnea in most patients with cardiopulmonary disease and disability.

JULIUS H. COMROE, JR., M.D.
Department of Physiology and Pharmacology
Graduate School of Medicine
University of Pennsylvania,
Philadelphia, Pa.

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For further information, write to Dr. Rafael Perez Diaz, Secretary, P. O. Box 2108, Havana, Cuba.

POSTGRADUATE COURSES FOR PHYSICIANS

A comprehensive list of postgraduate courses for physicians for the period September 1, 1956 to August 31, 1957, compiled by the Council on Medical Education and Hospitals of the AMA, appears in the July 28th issue of the Journal of the American Medical Association. The lists of courses in *Cardiovascular Disease*, in *Electrocardiography* and in *Peripheral Vascular Disease* are being reprinted in the news section of the October issue of Circulation. For courses in general practice, internal medicine, basic sciences and other special fields, the reader should consult the original list in the JAMA.